REMARKS/ARGUMENTS

Foreign Priority

The Office Action states the correct priority date – October 15, 2003 – for the application; however, it states that a certified copy of the priority Japanese application (JP 2003-354983) has not been filed with the application. A certified copy of JP 2003-354983 was filed with the PCT application and copy of this certified document was filed with the application. This document is listed on the IFW for this application.

Specification and Abstract

The Specification and Abstract have been amended to correct the cited problems with citations and translation. Additionally, the Specification has been rewritten to correct problems with grammar, style, verb tense and clarity. Even though the Specification has been extensively amended, no New Matter was added. The original priority Japanese application and PCT application were written in Japanese, so the US National application had to be translated into English. The originally filed English-translation, although correct in presenting the disclosed information, lacked the quality of a native English-speaker. The currently amended Specification presents the same disclosed information, but in a style that is easier to read.

Two versions of the Specification are submitted with this response. A "Marked-Up" version has been submitted showing all the amendments and corrections using the appropriate notation. A "Substitute Specification" has been submitted showing a "clean" version with all the amendments.

The Examiner is requested to remove the objections to the Abstract and Specification due to the cited informalities. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow the application.

Claim Objections - Claims 1, 3 - 4, 10 and 20 – 23

Claims 1 & 10

Claims 1 and 10 have been objected to due to the abbreviation "CTL" not being identified in the claims.

Original Claim 1 and 10 have been Canceled. New Claim 24 corresponds to Canceled Claim 1, and New Claim 25 corresponds to Canceled Claim 10. New Claims 24 and 25 identify the abbreviation "CTL" as "Cytotoxic T lymphocytes".

The Examiner is requested to remove the objections to the Claims due to the cited informalities. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 24 and 25.

Claims 3 - 4 and 20 – 23

The Office Action states that Claims 3 - 4 are substantially duplicated by Claims 20 – 23. The Applicants disagree with this conclusion; and Traverse.

Claims 3 & 4 are each dependent from Independent Claim 24; whereas:

Claim 20 is dependent from Claim 2, which is dependent from Claim 24;

Claim 21 is dependent from Claim 2, which is dependent from Claim 24;

Claim 22 is dependent from Claim 3, which is dependent from Claim 24; and

Claim 23 is dependent from Claim 20, which is dependent from Claim 2, which is dependent from Claim 24.

The differing dependencies [Claim Differentiation] of Claims 3, 4 and 20 – 23 show they are claiming different patent scope. The doctrine of Claim differentiation is based on "the common sense notion that different words or phrases used in separate claims are presumed to indicate that the claims have different meanings and scope (Karlin Tech v. Surgical Dynamics, Fed. Cir. 1999). Further, Tandon Corp. v. U.S. ITC (Fed. Cir. 1987) states "to the extent that the absence of such difference in meaning and scope would make a claim superfluous, the doctrine of claim differentiation states the presumption that the difference between claims is significant."

The Examiner is requested to remove the objection due to duplication of claims. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 3, 4, and 20 – 23.

Claims

35 USC § 112 ¶ 2 Rejections - Claims 1, 10 - 11 and 15 - 16

The Office Action rejected Claims 1, 10 - 11 and 15 - 16 under 35 USC § 112 ¶ 2 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24

New Claim 24 (corresponds to original Claim 1) claims a "drug kit for cancer therapy" and the components in the kit are listed.

Claim 25

New Claim 25 (corresponds to original Claim 10) is a method claim and gives each step in the method. Each step states the actions to accomplish the method.

The Office Action states "the claim [10] recites the intended infection of the carrier cell with an oncolytic virus. However, as presently written, the method does not require the cell to be infected with the oncolytic virus."

Step (c) of Claim 25 states ".. growing a carrier cell with an oncolytic virus to produce an oncolytic virus infected carrier cell ..", which corrects the cited problem.

Claim 11

The Office Action states "claim 11, it is unclear what the reference date is, e.g. about two to not more than thirteen weeks from what date and/or method step?

New Claim 25 in Step (b) states "waiting a period after administering the virus for immunological treatment before continuing with the method of cancer gene therapy" and Claim 11 claims this period as "within the range of about two weeks to not more than 13 weeks"

Claims 15 & 16

The Office Action states "claims 15-16, the claims are generally narrative and indefinite, failing to conform with current U.S. practice"

Claims 15 and 16 have been amended to correct informalities and errors in translation. Applicants believe the currently amended Claims 15 and 16 are in the proper form and style.

The Examiner is requested to remove the rejections under 35 USC § 112 ¶ 2. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 9 - 11 and 15 - 16, 24 and 25.

35 USC § 102(b) Rejection of Claims 1 - 3, and 20

The Office Action rejected Claims 1 - 3, and 20 under 35 USC 102(b) as being anticipated by Kikuchi *et al.* (Blood 100:3950-3959, 2002; available online July 25, 2002). The Office Action stated "Kikuchi *et al.* teach a drug kit for cancer therapy, the kit comprising a replication-deficient adenovirus and dendritic cells (pg 3951, Methods; pg 3953, col. 2, Synergistic anti-tumor effects)".

The Applicants disagree with the conclusion of the Office Action that Kikuchi *et al.* discloses, each and every feature, of Claims 1 – 3, and 20; and Traverse. New Claim 24 discloses a kit containing 3 ingredients: a virus for immunological treatment which is non-proliferative; a carrier cell which becomes infected with an oncolytic virus to produce an oncolytic virus infected carrier cell; and an oncolytic virus which is the same type of virus as the virus for immunological treatment and which is proliferative in the tumor cell.

A careful reading of Kikuchi *et al.* shows that it lacks any mention of "a virus for immunological treatment", "carrier cells", or "carrier cells infected with an oncolytic virus". None of the viruses disclosed in Kikuchi *et al.* are administered to an animal to induce an immunological reaction to the carrier cell. Additionally, Kikuchi *et al.* does not disclose a "carrier cell" or a "carrier cells infected with an oncolytic virus". The Office Action alleges that the twin treatment of first injecting AdNK4 into the tumor, and then waiting 3 days to inject DCs (bone marrow-generated dendritic cells) into the tumor is the same as administering "carrier cells infected with an oncolytic virus". This conclusion is incorrect, because the AdNK4 and the DCs are injected separately, the DCs are never infected with AdNK4, either *in vitro* or *in vivo*, and the purpose of injecting the DCs is to stimulate the immune system (see abstract, 2nd column, line 10 -12, Kikuchi *et al.*) not to deliver the oncolytic virus to the tumor.

The Examiner is requested to remove Kikuchi *et al.* as a 102(b) Prior Art reference. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 2, 3, 20 and 24.

35 USC § 102(e) Rejection of Claims 1 – 3, 10 – 12, 15 and 20

The Office Action rejected Claims 1 – 3, 10 – 12, 15 and 20 under 35 USC 102(e) as being anticipated by Terman, 2002/0177551 Al. The Office Action stated "With respect to claims 1 and 10, Terman discloses a cancer therapeutic drug and a method of treating tumors…, the method comprising a step of administering to a patient *in vivo* with a nucleic acid viral vector to induce a CTL reaction to a carrier cell expressing one or more desired antigens .., and after a predetermined period of time, the method further comprising a step of administering to said patient carrier cells infected with an oncolytic virus .."

The Applicants disagree with the conclusion of the Office Action that Terman '551 discloses, each and every feature, of Claims 1 and 10; and Traverse. New Claims 24 and 25 (corresponding to Claims 1 and 10) claim a kit and a method for cancer gene therapy. Claim 24 claims a kit containing a "virus for immunological treatment" to be administered to an animal and Claim 25 claims "administering a virus for immunological treatment to a patient". Terman '551 does not disclose a "virus for immunological treatment" or "administering a virus for immunological treatment to a patient".

Terman '551 discloses a method of inducing an immune reaction against SAg by using "cells transfected with nucleic acid that encodes a SAg polypeptide" [0051]. However, the SAg polypeptide does not confer oncolytic-activity to a virus. SAg is an immunostimulatory molecule and a "powerful T cell mitogen" [0010]. SAg are "capable of activating 5 to 30% or the total T cell population compared to 0.01% for conventional antigens" [0010]. Therefore, the production of SAg polypeptide by a transfected cell does not make the virus with SAg activity an "oncolytic virus". The name itself – oncolytic virus – describes the qualities a virus must have to be identified of this type. It is a virus that infects cancer cells and causes the cancer cells to lyse. Therefore, a virus with SAg cannot be called an oncolytic virus since it does not infect the cancer cell in the body and cuase the cancer cell to lyse.

Additionally, Terman '551 does not disclose any "virus for immunological treatment" that is to be used for administering to an animal (Claim 24) or a method of "administering a virus for immunological treatment to a patient" (Claim 25). All viruses disclosed by Terman '551 are used to transfect cells, rather than being directly administered to an animal or patient, without first being used to transfect a cell.

Claims 2 and 3 are dependent from Independent Claim 24, Claim 20 is dependent from Claim 3, and Claims 11, 12 and 15 are dependent from Independent Claim 25. Since Terman '551 does not anticipate Independent Claims 24 and 25, it further does not anticipate Claims 2, 3, 11, 12, 15, and 20, as these claims are dependent from the Independent claims.

The Examiner is requested to remove Terman '551 as a 102(e) Prior Art reference. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 2 – 3, 11 – 12, 15, 20, 24 and 25.

35 USC § 103(a) Rejection of Claims 1 – 4, 10 – 12, 15 and 20 - 23

The Office Action rejected Claims 1 – 4, 10 – 12, 15 and 20 – 23 under 35 USC 103(a) as being obvious over Terman (2002/0177551 Al) and Harrison *et al.* (Human Gene Therapy 12(10):1323-1332, 2001). The Office Action stated "Terman does not disclose the carrier cell to be an A549 cell. However, at the time of the invention, Harrison *et al.* taught the use of A549 cells to produce oncolytic adenoviruses in a method to treat tumors."

The Applicants disagree with the conclusion of the Office Action that the combination of Terman '551 and Harrison *et al.* discloses, each and every feature, of Claims 1 – 4, 10 – 12, 15 and 20 – 23, and makes them obvious; and Traverse.

As discussed above, Terman '551 does not disclose, each and every feature, of Independent Claims 24 and 25, and Harrison *et al.* does disclose those features which are deficient in Terman '551. Therefore, the disclosure of Harrison *et al.* is not sufficient to make obvious the claims dependent from Claims 24 and 25.

The Examiner is requested to remove the combination of Terman '551 and Harrison *et al.* as 103(a) Prior Art references. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 2 – 4, 11 – 12, 15 and 20 – 25.

35 USC § 103(a) Rejection of Claims 1, 6, 10 and 16

The Office Action rejected Claims 1, 6, 10 and 16 under 35 USC 103(a) as being obvious over Terman (2002/017755 1 Al) and Harrison *et al.* (Human Gene Therapy 12(10):1323-1332, 2001) claims 1 - 4, 10 - 12, 15 and 20 - 23 above, and in further view of Ochiya *et al.* (Curr. Gene Therapy 1: 31 - 52, 2001). The Office Action stated "The prior cited art does not teach the kit or method to comprise atelocollagen. However, at the time of the invention, Ochiya *et al.*

reviewed the advantages of using atelocollagen to mediate controlled-release of bioactive agents of molecular medicines."

The Applicants disagree with the conclusion of the Office Action that the combination of Terman '551, Harrison *et al.*, and Ochiya *et al.* discloses, each and every feature, of Claims 6 and 16, and makes them obvious; and Traverse.

As discussed above, Terman '551 does not disclose, each and every feature, of Independent Claims 24 and 25, and neither Harrison *et al.* nor Ochiya *et al.*, individually or in combination with Terman '551 disclose those features which are deficient in Terman '551. Therefore, the disclosures of Harrison *et al.* and Ochiya *et al.* are not sufficient to make obvious the Claims 6 and 16, which are dependent from Claims 24 and 25.

The Examiner is requested to remove the combination of Terman '551, Harrison *et al.* and Ochiya *et al.* as 103(a) Prior Art references. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 6, 16, 24 and 25.

35 USC § 103(a) Rejection of Claims 1 and 5

The Office Action rejected Claims 1 and 5 under 35 USC 103(a) as being obvious over Terman (2002/017755 1 Al), Harrison *et al.* (Human Gene Therapy 12(10):1323-1332, 2001), Ochiya *et al.* (Curr. Gene Therapy 1: 31-52, 2001), Alemany *et al.* (U.S. Patent 6,403,370 B1) and Barker *et al.* (Genomics 38:215-222, 1996). The Office Action stated "The prior cited art does not teach the oncolytic virus to comprise a 1A1.3B promoter. However, at the time of the invention, Alemany *et al.* disclosed a method for killing tumor target cells, the method comprising an oncolytic adenoviral vector, wherein the oncolytic adenoviral vector comprises a tumor cell-activated promoter operably linked to the adenoviral El gene. Alemany *et al.* do not disclose the use of a 1A1.3B promoter. However, at the time of the invention, Barker *et al.* taught that the identification of the promoter region for 1A1.3B and that 1A1.3B (also known as CAl25) is an art-recognized ovarian cancer marker antigen."

The Applicants disagree with the conclusion of the Office Action that the combination of Terman '551, Harrison *et al.*, Ochiya *et al.*, Alemany *et al.* and Barker *et al.* discloses, each and every feature, of Claims 1 and 5, and makes them obvious; and Traverse.

As discussed above, Terman '551 does not disclose, each and every feature, of Independent Claims 24, and neither Harrison *et al.*, Ochiya *et al.*, Alemany *et al.*, nor Barker *et al.*, individually or in combination with Terman '551, disclose those features which are deficient in Terman '551. Therefore, the disclosures of Alemany *et al.* and Barker *et al.* are not sufficient to make obvious Claim 5, which is dependent from Claims 24.

The Examiner is requested to remove the combination of Terman '551, Harrison *et al.*, Ochiya *et al.*, Alemany *et al.* and Barker *et al.* as 103(a) Prior Art references. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 5 and 24..

Double Patenting (Provisional) Rejection of Claims 1 – 6 and 20 - 23

The Office Action provisionally rejected Claims 1 - 6 and 20 - 23 under the judicially created doctrine of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1 - 5 of copending Application No. 10/575,894.

Applicants request this Provisional Rejection of nonstatutory obviousness-type double patenting be held in abeyance until the claims of copending Application No. 10/575,894 are examined and are in condition for allowance. It is unclear at this stage in the examination process of either application whether any claims in these applications will qualify for a rejection of nonstatutory obviousness-type double patenting at the time of allowance.

The Examiner is requested to hold in abeyance the Double Patenting Rejection. In light of the foregoing arguments and amendments to the claims, the Examiner is respectfully requested to allow Claims 2 – 6 and 20 – 24.

Amendments to Claims

No New Matter was added by the amendments to the Claims. All amendments to the claims were to correct errors in grammar, style and clarity, and not to narrow the claims to allow patentability over any cited references. The amended claims are claiming the same scope as the originally filed claims, and have not been narrowed by the amendments.

No Disclaimers or Disavowals

Although the present communication may include alterations to the claims, the Applicants are not conceding in this application that previously pending claims are not patentable. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

Conclusion

Claims 1 – 25 are pending. Claims 2 – 6, 11, 12, 15, 16, 20 – 23 are Currently amended. Claims 24 and 25 are New. Claims 7 – 9, 13, 14 and 17 – 19 are Withdrawn. Claims 1 and 10 are Canceled.

Payment of $60 is submitted with this response for a 1 month extension of filing the Response. No additional fees are believed due; however, the Commissioner is authorized to charge any additional fees now and in the future which may be due, including any fees for additional extension of time, or credit overpayment to credit card information.

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